

REMARKS

Claims 10-13, 15, and 19-24 are currently pending. Claims 10, 15, and 19 are amended herein. Applicants respectfully request entry of the amendments as they will place the claims in condition for allowance and/or place the claims in better form for appeal, if necessary.

Claim 10 has been amended to recite the abbreviations for von Willebrand factor (wVF), factor VIII:C (FVIII:C), factor VIII:C-containing von Willebrand factor complex (vWF/VIII:C), von Willebrand factor ristocetin cofactor activity (vWF:RCoF), and von Willebrand factor antigen (vWF:Ag). Likewise, claim 19 has been amended to recite the abbreviation for von Willebrand factor/factor VIII:C complex as "vWF/VIII:C," rather than "vWF:VIII:C," as previously presented. Support for these abbreviations can be found throughout the specification, for example, at page 1 line 11, page 2 lines 15-18, and page 4 lines 16-19. Thus, no new matter has been added.

To facilitate prosecution, and without acquiescing to the Office's rejection, Applicants have amended claim 15 to remove the term "precursor." This amendment should overcome the Office's 35 U.S.C. § 112, ¶ 2 rejection of claim 15.

Applicants acknowledge with appreciation the Office's withdrawal of the 35 U.S.C. § 112, ¶ 2 rejection of claim 12.

Claim Rejections Under 35 U.S.C. § 112 ¶ 1

In the Advisory Action, the Office maintained the rejection of claims 10, 15, and 19 as allegedly lacking enablement for "all amino acids and all metal salts." (February

8, 2006 Office Action at pages 3 and 7.) Applicants respectfully traverse and submit that the Office has failed to establish a *prima facie* case of nonenablement.

To satisfy the enablement requirement, the specification must enable a person of ordinary skill in the art to practice the claimed invention without undue experimentation. The Federal Circuit has held that making the claimed embodiments and screening them for function is acceptable, as long as the experimentation is not undue. Thus, the test is whether it would require undue experimentation to practice the invention. See generally, *Atlas Powder v. E.I. Du Pont de Nemours & Co.* 750 F.2d 1569, 224 U.S.P.Q. 409 (Fed. Cir. 1984). Furthermore, MPEP § 2164.06 states, “the test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.” MPEP § 2164.06 citing *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (emphasis added).

Applicants submit that the level of skill and predictability in the art at the time of filing was high. Fractional precipitation methods were known to one of ordinary skill in the art and the specification provides ample guidance with respect to any necessary experimentation. Examples of such teachings include:

- Choice and preparation of starting material, described on pages 6-7 of the specification;
- Method for obtaining the concentrate of the invention by precipitation, including particular concentration ranges of precipitants, described on pages 7-9;

- Example 1 (specification at pages 9-11), which teaches fractional precipitation of the vWF/FVIII:C concentrate, analysis of the precipitates for vWF:RCoF activity (which measures the functional activity of vWF), and measurement of vWF:Ag and FVIII:C concentrations;
- Example 2 (specification at pages 11-14), which teaches a first and a second precipitation, each precipitation followed by a measurement of vWF activity;
- Example 3 (specification at pages 14-16), which teaches precipitation of the vWF/FVIII:C fraction with the same NaCl/glycine concentration, but with varying addition and incubation times;
- Example 4 (specification at pages 16-18), which teaches fractional precipitation of the vWF/FVIII:C concentrate and, at the same time, teaches a first and second precipitation;
- Example 5 (specification at pages 18-21), which teaches stabilization, sterilization, and lyophilization of a fraction enriched with high molecular weight vWF multimers, and the production of a vWF/FVIII:C concentrate in which the vWF high molecular weight markers were reduced; and
- Example 6 (specification at page 22), which demonstrates fractional precipitation of high molecular weight vWF multimers from a supernatant containing recombinant FVIII:C and plasma vWF.

In light of the large amount of guidance provided in the specification regarding production of a concentrate and optimization of conditions, the amount of experimentation would not be undue. In *United States v. Telectronics, Inc.*, 857 F.2d

778 (Fed Cir. 1988), the court ruled that since one embodiment and the method to determine efficacy were set forth in the specification, the specification was enabling. The instant specification discloses the use of glycine and NaCl and describes methods to optimize their use in producing a concentrate of a factor VIII:C-containing von Willebrand factor. Furthermore, the scope of claim 10 does not include "all metal salts," as alleged by the Office, and instead recites "an alkali metal and an alkaline earth metal salt." Thus, the species of amino acids and alkali metal or alkaline earth metal salts taught in the specification and recited in claim 10 can be easily tested to select the conditions that result in an increased content of functional, high molecular weight vWF multimers.

Therefore, since no undue experimentation is required, Applicants respectfully request that the Office withdraw the rejection of claim 10 and its dependent claims 15 and 19, for allegedly failing to enable "all amino acids and all metal salts."

In the Advisory Action, the Office also maintained the rejection of claim 15 as allegedly lacking enablement because "the conditions for the stabilization and pasteurization of the concentrate or the concentrate precursors should be provided." (February 8, 2006 Office Action at page 4.)

Regarding recitation of the conditions for stabilization, Applicants again refer the Office to the Amendment dated May 3, 2006, in which claim 15 was amended to recite stabilization conditions of "at least one of sucrose, glycine, calcium ions, and albumin." The Office entered the amendment, but has not offered any explanation as to why the previous amendment to claim 15 does not overcome the present rejection. Without

such guidance, Applicants are left to speculate as to the basis for the rejection. As previously stated, in view of this amendment and the teachings in the specification (discussed on page 7 of the May 3, 2006 Amendment) one of skill in the art would be able to both make and use a more stable factor VIII:C-containing von Willebrand factor concentrate or concentrate precursor.

Regarding recitation of the conditions for pasteurization, Applicants respectfully traverse. Pasteurization is a well-known technique. The specification, for example at page 9 line 10, teaches one embodiment of pasteurization as “heat[ing] at 60°C for 10 hours.” Other embodiments were known in the art at the time of filing the instant application. For example, Exhibit A teaches that pasteurization “consists of heating at 62°C for 30 minutes or, in ‘flash’ pasteurization, at a higher temperature for a fraction of a minute.” (Page 1265 left column through page 1266 right column.) Thus, given the high predictability of the art, the general knowledge of pasteurization techniques, and the specific embodiment of pasteurization described in the instant specification, the specification fully enables one skilled in the art to practice the invention as claimed. Limiting claim 15 to specific pasteurization conditions is unnecessary, as undue experimentation would not be required to practice the instantly claimed invention.

In view of the previously presented amendment to claim 15 and foregoing discussion, Applicants respectfully request that the Office withdraw the enablement rejection of claim 15, for allegedly failing to recite stabilization and pasteurization conditions.

Claim Rejections Under 35 U.S.C. § 112 ¶ 2

In the Advisory Action, the Office maintained the rejection of claim 10 as allegedly being indefinite because “the value for the ratio ‘greater than 1’ is not provided . . . [and] a reasonable range should be provided to make the claim definite.” (February 8, 2006 Office Action at page 6.) Applicants respectfully traverse.

A ratio of the vWF:RCoF activity to the vWF:Ag concentration of “greater than 1” would be understood by a practitioner of ordinary skill in the art in light of the specification. One of ordinary skill in the art would clearly recognize that claim 10 requires that the vWF:RCoF activity is greater than the vWF:Ag concentration. The boundary of the claim is clear, as a vWF:RCoF activity that is less than or equal to the vWF:Ag concentration does not meet the requirements of claim 10. Thus, the ratio of “greater than 1” language of claim 10 fulfills definiteness requirement.

Furthermore, Applicants submit that the Office has not explained why the “greater than 1” claim language does not have a reasonable degree of clarity and why a “reasonable range should be provided.” Applicants respectfully submit that the “greater than 1” claim language is clear and precise and fulfills the purpose of the definiteness requirement. As recited in claim 10, the value for the ratio of vWF:RCoF activity to vWF:Ag concentration has a clearly defined lower limit of 1. This limitation requires that the numerator (vWF:RCoF activity) is greater than the denominator (vWF:Ag concentration). Since a ratio is a comparison of two quantities, it is neither appropriate, nor necessary to specify a range of values for the ratio when the desired result is simply

that one quantity in the ratio be greater than the other. Therefore, Applicants request that the Office withdraw the indefiniteness rejection of claim 10.

In the Advisory Action, the Office also maintained the rejection of claim 15 because the term "precursor" is allegedly indefinite "since the structure or name of the precursor is not provided in the claim." (February 8, 2006 Office Action at page 6.) To facilitate prosecution, and without acquiescing to the rejection, claim 15 has been amended to remove the term "precursor." Thus, Applicants respectfully request that the indefiniteness rejection of claim 15 be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request that this Amendment under 37 C.F.R. § 1.116 be entered by the Office, thereby placing claims 10-13, 15, and 19-24 in condition for allowance. Applicants submit that the proposed amendments of claims 10, 15, and 19 do not raise new issues or necessitate the undertaking of any additional search of the art by the Office, since all of the elements and their relationships claimed were either earlier claimed or inherent in the claims as examined. Therefore, this Amendment should allow for immediate action by the Examiner. Finally, Applicants submit that the entry of the amendment would place the application in better form for appeal, should the Office dispute the patentability of the pending claims.

In view of the foregoing remarks, Applicants submit that this claimed invention, as amended, is both enabled and the claim language is definite. Applicants therefore request the entry of this Amendment, the Office's reconsideration and reexamination of the application, and the timely allowance of the pending claims.

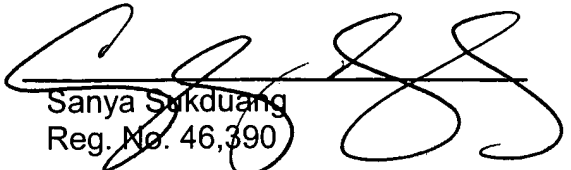
Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

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By


Sanya Sukduang
Reg. No. 46,390